

## REMARKS

Claims 1-10 and 44 were pending prior to this Response. By the present communication, no claims have been added or cancelled, and claim 1 has been amended to define the invention with greater particularity. The new claim language adds no new matter, being fully supported by the Specification and original claims. Accordingly claims 1-10 and 44 are currently pending.

### The Issue of New Matter

The Advisory Action asserts that the amendment to claim 1 included in the Response to the Final Office Action filed on January 20, 2004, namely the phrases “capillaries fixedly held together in an array” and “a lumen for retaining a sample by capillary forces”, potentially introduce the issue of new matter. Claim 1 has been further amended to replace the phrase “fixedly held together” with the phrase “permanently bound together”. Support for the new claim language “permanently bound together” is found in the Specification at page 5, paragraph [0029] which recites, in part: “The capillaries (20) can be bound together, by being fused (*e.g.*, where the capillaries are made of glass), glued, bonded, or clamped side-by-side. . . .” In addition, support for the phrase “a lumen for retaining a sample by capillary forces” is found in the Specification, which recites:

The liquid is wicked into the capillary tubes by capillary action. The natural wicking that occurs as a result of capillary forces obviates the need for pumping equipment and liquid dispensers. A substrate for measuring biological activity (*e.g.*, enzyme activity) can be contacted with the particles either before or after introduction of the particles into the capillaries in the capillary array. The substrate can include clones of a cell of interest, for example. The substrate can be introduced simultaneously into the capillaries by placing an open end of the capillaries in the container (100) containing a mixture of the particle-bearing liquid and the substrate.

(page 9, paragraph [0044]). See also the **Abstract**, which recites: “Each capillary includes at least one wall defining a lumen for retaining the detectable sample. The detectable sample is introduced to and retained in the lumen by capillary forces.” Thus, Applicants

respectfully submit that the amendment to claim 1 does not constitute new matter, and examination of the claims as amended herein is respectfully requested.

### **The Objection to the Specification**

Applicant respectfully traverses the rejection of the Specification on the grounds that an amendment to paragraph 0006 adds new matter by adding “optionally” and deleting “within” in the phrase “and optionally, one or more reference indicia formed ~~within~~ the interstitial material.” The Examiner asserts that Applicant did not point to support in the originally filed specification for these changes and new definitions (Final Office Action, page 3).

To correct an error inadvertently introduced by amendment, paragraph 0006 was amended in the Response to the Final Office Action to recite: “and optionally, one or more reference indicia disposed within the interstitial material.” Support for this amendment to paragraph 0006 is found in paragraph 0038 of the original Specification, which describes reference indicia as “optional” and “formed of a pad of glass extending from the surface of the capillary array, or embedded in the interstitial material . . . .” In view of the amendment to paragraph 0006 made in the Response to the Final Office Action and the support for the amendment provided above, Applicant respectfully submits that grounds for the objection are obviated. Accordingly, reconsideration and withdrawal of the objection to the Specification are respectfully requested.

### **The Rejection under 35 U.S.C. § 102(a)**

A. Applicant respectfully traverses the rejection of claims 1-7 under 35 U.S.C. § 102(a) as being anticipated by Kumar et al (WO 98/04920; hereinafter “Kumar”). The invention sample screening apparatus, as defined by amended claim 1, distinguishes over the disclosure of Kumar by requiring “a plurality of parallel capillaries permanently bound together in an array, wherein each capillary comprises at least one wall defining a lumen for retaining a sample by capillary

forces; and interstitial material disposed between adjacent capillaries in the array.” As used in Applicant’s Specification and claims, the term “interstitial material” means material in the spaces or interstices between the capillaries that acts to bind the capillaries permanently together. This meaning is in keeping with the dictionary definitions of “*interstitial*” and “*interstice*: A space, esp. a small or narrow one, between things or parts” *Webster’s II New College Dictionary*, Houghton Mifflin Company, 1995. In one embodiment, the interstitial material is glass fused to the exterior of the glass capillaries. In another embodiment, the interstitial material is glue applied to the exterior of the capillaries, which binds the capillaries together permanently. Thus, the interstitial material can function to permanently bind the capillaries together.

Kumar is absolutely silent regarding an array wherein the capillaries are permanently bound together, for example by interstitial material. The Examiner relies upon Kumar’s disposable cartridge as evidence that Kumar discloses “interstitial material”. However, Kumar discloses capillary tubes held only at the top edge within a disposable cartridge. As can be seen from the cover page drawing of Kumar, the positioning of the capillary tubes does not create interstices that are filled with interstitial material. In addition, the capillary tubes are not permanently bound via Kumar’s cartridge holder because Kumar’s capillary tubes are designed to be removed from the cartridge at will. Thus, Kumar fails to disclose at least two key elements of the invention screening apparatus, as defined by amended claim 1.

To establish anticipation under 35 U.S.C. § 102, each and every element of a claim must be found in a single reference. Since Kumar fails to disclose each and every element of amended claim 1, the reference fails to anticipate claims 1-7. Accordingly, reconsideration and withdrawal of the rejection over Kumar are respectfully requested.

**B.** Applicant respectfully traverses the rejection of claims 1-7 under 35 U.S.C. § 102(a) as being anticipated by Dehlinger (U.S. Patent No. 5,763,263). The invention sample screening apparatus, as defined by amended claim 1, distinguishes over the disclosure of Dehlinger by

requiring “a plurality of parallel capillaries permanently bound together in a non-uniform array, wherein each capillary comprises at least one wall defining a lumen for retaining a sample by capillary forces; and interstitial material disposed between adjacent capillaries in the array.”

Thus, Applicant submits that the amendment to claim 1 overcomes the Examiner’s assertion that Applicant’s argument regarding the differences between the invention capillary array and that disclosed by Dehlinger is inadequate.

The invention array, as defined by amended claim 1, is “non-uniform” in arrangement (See Figure 1B and paragraph 36, line 3 for support for this term) such that the capillaries do not line up into perfect rows and columns as is the case in an “addressable” array. Those of skill in the glass drawing arts, would understand that the method of making the invention arrays, as described by paragraphs 32 and 33, inherently results in an array that is “non-uniform” and which cannot be scanned or “read” using the type of technology employed when an array is “position-addressable.”

By contrast, Dehlinger is absolutely silent regarding a “non-uniform array wherein the capillary lumen retains liquid reactants by capillary forces. Instead, Dehlinger discloses a “position-addressable” array used for building a reactant, such as a chemical compound or a polymeric substance, in incremental steps within a capillary wherein the reactant under construction is tethered to the interior wall of the capillary by a chemical linker (Dehlinger does not say how the chemical linker is applied to the interior wall of the capillary). Dehlinger’s method of constructing a combinatorial library dictates that the capillaries be in a uniform arrangement, for example, of rows and columns so that automated equipment can be used to deposit known reactants into known subsets of capillaries.

In addition, Applicants again point out that in the invention capillary array, as defined by amended claim 1, the capillaries are sized such that liquid reactants are subject to capillary forces and are retained within the capillary array by capillary forces. In certain embodiments, the capillaries are tubes open at both ends and the reactants are “imbibed” into the tubes without

the need for pumping simply by submerging the open end of the capillaries into a bath containing one or more of the reactants. Applicants also teach that the capillary forces holding the liquids in the tube can be separated by a bubble of air, which can be broken by applying pressure to the end of the tube to break the bubble. This phenomenon is possible only because the liquid reactants are held within the capillaries by capillary forces. (See Specification, pages 13-14, paragraphs [0051] – [0053]).

By contrast, Dehlinger's reactants are linked to the internal walls of the capillaries. FIG. 8 is "an enlarged sectional view of a capillary tube in a tube array, showing a central wall portion with attached linkers on which to build molecules of a library compound" (Brief Description of the Drawings). Certain of the compounds that go into building up the reactant may be imbibed into capillaries in the array as shown in Fig. 4A but the growing molecule is tethered to the interior of the capillary tube.

In view of these differences between the invention arrays and those described by Dehlinger, Applicant submits that Dehlinger fails to disclose each and every element of the invention screening apparatus, as defined by amended claim 1. To establish anticipation under 35 U.S.C. § 102, each and every element of a claim must be found in a single reference. Since Dehlinger fails to disclose each and every element of amended claim 1, Applicant requests reconsideration and withdrawal of the rejection over Dehlinger.

#### **The Rejection under 35 U.S.C. § 103(a)**

A. Applicant respectfully traverses the rejection of claims 8-10 and 44 under 35 U.S.C. § 103(a) for being unpatentable over Kumar in view of Winkler et al. (U.S. Patent No. 5,677,195; hereinafter "Winkler"), as allegedly being unpatentable. Applicant respectfully submits that remarks above with regard to the differences between Kumar and the invention defined by claims 1-7 apply equally to dependent claims 8-10 and 44 and are incorporated here.

Kumar is absolutely silent regarding an array wherein the capillaries are permanently bound together, for example by interstitial material.

Moreover, Applicant submits that due to Kumar's emphasis upon removable tubes held in a cartridge, those of skill in the art would not be motivated by Kumar to adapt the disclosed apparatus along the lines of the invention sample screening apparatus to provide an array wherein the capillaries are permanently bound together by interstitial material for addressable screening. Kumar's tubes are designed to fit into holes provided in a device that is used to individually analyze the contents of the capillary tubes. Thus, there is no reason provided by the reference itself to add positionally addressable indicia to the Kumar advice because such indicia are not needed.

In addition, Applicant submits that the combination of Kumar and Winkler would not motivate those of skill in the art to design the invention sample screening apparatus. The array disclosed by Winkler is not an array of capillaries, but is instead a flat, optionally rotatable "substrate" having discrete "reaction regions" defined thereon into which a series of monomers are sequentially deposited to fabricate a substance for testing. For example, Winkler teaches that "reagents are delivered to the substrate by either (1) flowing within a channel defined on predefined regions or (2) 'spotting' on predefined regions" (Col 8, lines 64-67). Alternatively, a single molecule, such as a "receptor" can be attached to each region of the substrate and then subjected to a battery of putative binding agents or ligands for the receptor on the flat array. Because Winkler discloses that array components are deposited at locations on a two dimensional array from pipettes or flow-through channels, there is no suggestion in Winkler of an array of capillary tubes or of tubes dimensioned to load *and retain* an analyte by capillary forces. In particular, Winkler fails to suggest a cultivation of a clone with a substrate within a capillary tube. Thus, Winkler's disclosure regarding use of reference indicia at array intervals or edges in addressable arrays does not cure the deficiencies of Kumar for suggesting the invention apparatus, as defined by claims 8-10 and 44.

Nor do the references themselves suggest how to modify Kumar's device to provide the invention position-addressable capillary array with capillaries permanently bound together by interstitial material because neither reference refers to or suggests interstitial material (e.g., permanently) placed between adjacent capillaries in an array. Consequently, neither reference suggests that interstitial material can be marked with reference indicia. In addition, Winkler's disclosure regarding a positionally addressable flat substrate upon which molecules are synthesized in a grid pattern, even in combination with Kumar's disclosure of an array that looks like a row of test tubes in a test tube holder, would not be sufficient to motivate those of skill in the art to dispose indicia within an interstitial medium fixedly holding capillaries together.

Thus, Applicant respectfully submits that, even if the combined disclosures of Kumar and Winkler can be said to suggest creation of a position-addressable array, the subject matter of present claims 8-10 and 44 is not suggested under 35 U.S.C. § 103. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

**B.** Applicant respectfully traverses the rejection of claims 8-10 and 44 under 35 U.S.C. § 103(a) for being unpatentable over Dehlinger in view of Winkler as allegedly being unpatentable. Applicant respectfully submits that remarks above with regard to the differences between Dehlinger and the invention defined by claims 1-7 apply equally to dependent claims 8-10 and 44 and are incorporated here. In addition, Applicant submits that the combination of Dehlinger and Winkler fails to suggest the invention position addressable array of claims 8-10 and 44.

Dehlinger discloses a "position-addressable" array of capillary tubes suitable for use of capillary action to repetitively "imbibe" individual monomers (e.g., nucleotides) to be used in synthesis of the reagents, but Dehlinger neither discloses nor suggests designing a "non-uniform" capillary array with capillary lumens designed to retain an analyte by capillary forces. Moreover, Applicant submits that Dehlinger would not motivate those of skill in the art to modify the disclosed array to make it suitable for Applicant's invention because Dehlinger's

invention is focused on a method for building a combinatorial library of molecules, not for testing of already existing molecules. Moreover, even if those of skill in the art were motivated by Dehlinger to adapt the disclosed "position-addressable" array along the lines of Applicant's "non-uniform" array, there would be no reasonable expectation of success because it would not be possible to use a non-uniform array for construction of Dehlinger's massive parallel synthesis compound library. Moreover, Dehlinger fails to disclose any method by which a "non-uniform" array could be read since Dehlinger's description is focused on assay of the molecules by having a "position addressable" array, wherein the identity of a molecule that presents a positive reaction is known by knowing in advance the combination of analytes that has been introduced into each capillary of the array.

Moreover, addition of Winkler's disclosure relied upon by the Examiner pertains to use of reference indicia on a flat tray. Thus addition of Winkler's disclosure to the description of Dehlinger fails to suggest the invention methods or to overcome the deficiencies of Dehlinger such that the combination of Dehlinger and Winkler would suggest the invention sample screening apparatus to those of skill in the art. The remarks above concerning Winkler apply equally and are incorporated here.

Applicant submits that Winkler's disclosure regarding a positionally addressable flat substrate upon which molecules are synthesized in a grid pattern would not motivate those of skill in the art to modify Dehlinger's capillary array to add reference indicia within an interstitial medium permanently binding a plurality of capillaries into a "non-uniform" array. Winkler's disclosure is focused upon deposition of reactants at regularly arranged locations on a two dimensional substrate.

In addition, Winkler's disclosure regarding detection of molecules on a flat positionally addressable substrate with molecules synthesized in a grid pattern appears to be "addressed" in terms suitable to a flat array (i.e., certain areas of the substrate where light paths intersect are brighter than others, indicating the presence of a particular oligomer formed there (See Section D



Channel Matrix Hybridization Assay, Col 29-30), but does not suggest how to adapt the concept of using reference indicia to a to Dehlinger's three dimensional array.

Moreover, Winkler detection system is no more suitable to a 'non-uniform' array than is Dehlinger's so that the combined disclosures of Dehlinger and Winkler would fail to provide those of skill in the art with a reasonable expectation of success in using a non-uniform capillary array to detect optical signals.

Thus, Applicant submits that the subject matter of present claims 8-10 and 44 is not suggested under 35 U.S.C. § 103 by the combined disclosures of Dehlinger and Winkler and reconsideration and withdrawal of the rejection are respectfully requested.

#### **The Double Patenting Rejection**

The rejection based on double patenting of the "same invention" type under 35 U.S.C. § 101 has been maintained despite Applicant's filing of a Terminal Disclaimer over application Serial No. 09/790,321 on the grounds that a statutory type double patenting rejection cannot be overcome by filing of a Terminal Disclaimer. However, Applicant respectfully submits that claims 1-10, as amended herein, are not co-extensive with claims 1-10 of application Serial No. 09/790,321. Therefore, in view of the Terminal Disclaimer filed, Applicant respectfully requests reconsideration and withdrawal of the rejection of claims herein based on double patenting of the "same invention" type under 35 U.S.C. § 101.

In view of the above amendments and remarks, Applicant respectfully submits that all rejections have been overcome and allowance of claims 1-10 and 44 is respectfully requested.

In re Application of:  
William Michael Lafferty  
Application No.: 09/894,956  
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Page 13

PATENT  
Attorney Docket No.: DIVER1280-14

If the Examiner would like to discuss any of the issues raised in the Office Action, the Examiner is encouraged to call the undersigned so that a prompt disposition of this application can be achieved.

Respectfully submitted,

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